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MEDICAL RESEARCH COMMITTEE.

REPORTS

OF THE

CHEMICAL WARFARE MEDICAL COMMITTEE.

No. 13.—BLEEDING AFTER POISONING
BY PULMONARY IRRITANT GASES,
WITH APPENDICES.



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November, 1918.

In January, 1918, the Director-General, Army Medical Service, with the concurrence of the Controller of the Chemical Warfare Department, Ministry of Munitions, appointed the following Committee to prepare reports, based upon information received from all sources at the Chemical Warfare Department, for submission to him with a view to their distribution to those concerned, to make suggestions for further co-ordinated medical investigations that may seem desirable, and to advise him generally in respect of the scientific medical aspects of Chemical Warfare :—

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(With the co-operation of Lieut.-Colonel C. Gordon Douglas, M.C., M.D., R.A.M.C., and Colonel T. R. Elliott, D.S.O., M.D., F.R.S., in France, and of other corresponding members at Porton and in London, Edinburgh, France and Italy.)

REPORTS ALREADY ISSUED.

No. 1. Notes on the Pathology and Treatment of the Effects of Pulmonary Irritant Gases. (*March*, 1918.)

No. 2. The Histological Effects produced by Gas Poisoning and their Significance. (*April*, 1918.)

No. 3. The Symptoms and Treatment of the late Effects of Gas Poisoning. (*April*, 1918.)

No. 4. Polycythæmia after Gas Poisoning and the Effect of Oxygen Administration in the Treatment of Chronic Cases. (*April*, 1918.)

No. 5. The Reflex Restriction of Respiration after Gas Poisoning. (*April*, 1918.)

No. 6. Investigations into the Reaction of the Blood after Gas Poisoning, and the Results of the Administration of Saline and other Substances. The Effects of Bleeding and of the Injection of Calcium Chloride. (*April*, 1918.)

No. 7. Changes observed in the Heart and Circulation and the general After-Effects of Irritant Gas Poisoning. (*April*, 1918.)

No. 8. Reports on Fatal Cases of Poisoning. (i) Ethyl iodacetate. (*June*, 1918.)

No. 9. Tissue Changes in Animals produced by Pulmonary Irritant Gases. (*September*, 1918.)

No. 10. The Administration of Oxygen in Irritant Gas Poisoning. (*October*, 1918.)

No. 11. Investigations of Chronic Cases of Gas Poisoning. (*October*, 1918.)

No. 12. Treatment of Patients suffering from "Effort Syndrome" by Continuous Inhalation of Oxygen. (*October*, 1918.)

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BLEEDING AFTER POISONING BY PULMONARY IRRITANT GASES.

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BLEEDING AFTER POISONING BY PULMONARY IRRITANT GASES.

(Report by the C.W.M.C., September 25th, 1918.)

I. INTRODUCTION.

BEFORE discussing the question of "bleeding" we desire to state that in this report we are not concerned with the *comparative* values of oxygen administration and bleeding as lines of treatment.

Though the unanimous opinion of medical officers has been that bleeding often produces immediate relief of the condition resulting from irritant gas poisoning, there is still a lack of precise knowledge as to the nature of the benefit brought about. It is the purpose of the present report to review the evidence supporting the value of bleeding, and to make any practicable suggestions that seem justifiable as to the part it plays in the amelioration of the gassed state.

Some have attributed the importance of bleeding chiefly to relief of dangerous over-distension of the right side of the heart, which itself is the consequence of obstruction to the pulmonary bloodflow owing to alterations in the vascular bed caused primarily by anoxæmia or damage to the lung capillaries. This is doubtless the explanation of the immediate relief afforded to the asphyxial cases, described later. The resistance to the flow from the right side of the heart leads to venous engorgement, the thoracic and abdominal veins become distended, and with the general venous retardation that results one may connect the capillary distension shown in a large number of gassed cases, constituting the distinctive mark of the so-called "blue" or "plum-coloured" cases. At the commencement of this asphyxial stage the heart is working effectively; but the heart may later fail. The venous tension then becomes less evident, and a case may pass, gradually or suddenly, into another category, that of the "grey" or collapsed cases, *i.e.*, the asphyxial condition present is not accompanied by venous and capillary distension.

But the relief afforded by venesection may depend, as some have held, upon a change in another factor of the mechanics of the blood-flow, *viz.*, the viscosity of the blood. One effect of bleeding, at any rate in a normal individual, is to dilute the blood, since after bleeding the blood takes up liquid from the tissues. The viscosity therefore tends to become diminished. As the result, the circulation through obstructed pulmonary areas is presumably facilitated and the increased rate of flow may more than compensate for the diminished oxygen-carrying capacity of the blood. In this way bleeding may furnish relief to the anoxæmia which exists.

Finally, it has been thought that bleeding may operate preventively against the onset of pulmonary oedema or may be curative in that it tends to reduce the oedema after it is established.

The evidence is comprised mainly in the following clinical and scientific contributions to knowledge.

- (1) The effects of nitrous fumes in mines noted by Macaulay and others in South Africa and Australia and summarized by Irvine.*
- (2) J. S. Haldane's memorandum.†
- (3) Experimental studies of W. M. Bayliss.‡
- (4) Experimental studies at Porton by Capts. Dunn and Hunt.||
- (5) Experimental studies at Porton by Maj. Boycott and Capt. Hunt.§
- (6) Experimental studies (partly at Porton) by F. P. Underhill and Lieuts. Goldschmidt and Wilson.¶
- (7) Clinical evidence forwarded to C.W.M.C. by Maj.-Gen. Sir W. Herringham.
- (8) Medical report of Capt. Hebblethwaite.**
- (9) Views of French medical authorities.††
- (10) Views of German medical authorities.‡‡

The views expressed by other authorities at different Allied medical conferences in France have also been communicated to us by Lt.-Col. C. G. Douglas and others.

II. REVIEW OF EXPERIMENTAL EVIDENCE.

(1) *The Experiments of W. M. Bayliss.*

The animals (cats) were intensely gassed with chlorine. A fall of arterial blood-pressure resulted proportionate to the concentration of the chlorine. With a concentration of 1 in 2,000, the fall may amount to 50 per cent. The fall of blood-pressure preceded the lung œdema. Removal of one-seventh to one-tenth of the volume of the blood (early, before lung œdema had set in) caused a further fall of blood-pressure. Later the animals recovered from this second fall, but the blood-pressure did not rise above the level caused originally by the chlorine. Removal of blood, after the lung œdema had set in, caused a fall of blood-pressure which was persistent. Removal of blood also lowered the venous blood-pressure.

The conclusion arrived at was that the early removal of blood was of no benefit, later removal hastened death. It seems possible that in Bayliss's cases we have cases so intensely affected as to be analogous to the "grey" cases of medical practice.

(2) *The Experiments at Porton by Maj. Boycott, Capts. Dunn and Hunt.*

These experiments were undertaken to attempt to answer the question "Does bleeding notably reduce the amount of *pulmonary œdema* resulting from gas poisoning?"

* Irvine. B.M.J., 1916, i, 162.

† Haldane. B.M.J., 1917, i.

‡ Bayliss. Reports of the C.W.M.C., No. 6.

|| Dunn & Hunt. Reports of the C.W.M.C., present number, Appendix 1.

§ Boycott & Hunt. Reports of the C.W.M.C., present number, Appendix 2.

¶ Underhill, Goldschmidt & Wilson. Reports of the C.W.M.C., present number, Appendix 3.

** This is summarized in the B.M.J., 1916, ii, 107.

†† Confidentially circulated in May, 1918.

‡‡ From translation of captured German document of about January, 1918.

The effects of the bleeding were judged by the condition of the lung and the lung-heart ratio. Chloropicrin and phosgene were the gases. The former was used in the proportion of 1/21,500, the latter 1/6,000 to 10,000, the exposure being 20 to 30 minutes. Bleeding in 3, 6 or 24 hours did not affect the ultimate œdema.

With smaller doses of the gases (phosgene 1/10,000, and chloropicrin 1/40,000 for 15 or 20 minutes) the evidence was that, perhaps, there was some slight advantage in bleeding after phosgene, but none was shown after chloropicrin.

The conclusion arrived at, judging by the development of pulmonary œdema, was that there was no very obvious advantage in "bleeding."

(3) *The Experiments of Underhill and 1st Lieuts. Goldschmidt and Wilson, San. Corps, U.S.N.A.*

These experiments were designed to answer the question, "Does 'bleeding,' and other subsidiary treatment increase the expectation of life in a gassed animal?"

The results of the experiments are set out in the annexed table, and it is apparent that they have been carried out on a much larger scale than others.

	Acute deaths (within three days).	Secondary deaths.	Survivals.
<i>A. Animals gassed with Chlorine.</i>	Per cent.	Per cent.	Per cent.
(1/1,200 for 30 minutes.)			
23 dogs, not further treated	87	4	9
20 dogs, bled only (within 2 hrs.)	65	5	30
62 dogs, bled, immediately infused with equal quantity of saline and given 200 cc. of 5 per cent. NaHCO_3	53	23	24
<i>B. Animals gassed with Chloropicrin.</i>			
(1/9,000 for 25 minutes.)			
48 goats, untreated	90		10
47 goats, bled only (one hour after gassing)	57		43
<i>C. Animals gassed with Phosgene.</i>			
(1/13,500 for 30 minutes.)			
27 dogs, untreated	67	11	22
30 dogs, bled one hour after gassing	40	10	50
30 dogs, bled five hours	43	10	47
35 dogs, bled and immediately infused with saline	50	3	47
35 dogs, bled and infused 15 hours after bleeding	31	17	52
17 dogs <i>not</i> bled but immediately infused with saline	71	0	29

The animals that were bled had blood removed to the extent of 1 per cent. of their body weight. Infusion consisted in injecting sterile saline (isotonic) in quantity equal to the amount of blood removed.

These observers lay stress on the importance of the time of death should it occur. If the animal does not die within three days they regard it as surviving the immediate effect of the gassing, but in assessing the absolute value of a line of treatment, we are disposed to attach most importance to its success in achieving ultimate recovery.

We may, apparently, neglect the dosing with 10 grammes of sodium bicarbonate as materially altering the condition of the animal, and regard the 62 dogs in A. as merely bled and infused. We infer, therefore, that the immediate infusion with saline after "bleeding" did not favourably influence the prospect of ultimate survival, as compared with "bleeding" alone, either after chlorine or phosgene (C). There is no information available as to the blood pressure in the dogs in A., but the concentration of the chlorine is such as to lead us to regard these dogs as being less severely gassed than Bayliss's cats.

The goats treated by "bleeding" show a remarkable increase of survivals, 43 per cent. against 10 per cent. (It should be mentioned that the survivors were killed seven days after gassing, but goats surviving for this period almost invariably recover.) *These experiments strongly support the value of "bleeding" in severe cases.* No information is afforded as to whether a condition of venous engorgement was present.

In Table C. (phosgene experiments) "bleeding," either one hour or five hours after gassing, raises the survival rate from 22 per cent. to 50 per cent. "Bleeding," therefore, is shown to have a marked value. The immediate infusion with saline appears to be of no favourable influence; but the evidence at present available as to the results of delayed infusion indicate that the effect of such infusion is to postpone death from the "acute" period to the "secondary" period though not appreciably to increase the survival rate.

Later observations of the American investigators indicate that if infusion be practised at a time when the blood begins to exhibit concentration the effect upon survival is more beneficial than when performed at the fixed period of fifteen hours. As infusion at this interval does not at any rate diminish the beneficial effect of bleeding alone it may be inferred that bleeding plus infusion at the appropriate time has advantages over bleeding alone.

The principal conclusions at which the American workers have arrived are :—

- (1) Bleeding is beneficial for animals gassed with either chlorine, chloropicrin or phosgene, three typical examples of the class of lung irritants.
- (2) In so far as animal experiments may indicate, general application of bleeding to gassed men seems justifiable, and on the basis of these results the following recommendations are made.
- (3) Early bleeding is advisable in severely gassed cases. The lighter the gassing the more delay is possible.

- (4) Repeated small bleedings may be resorted to in lighter forms of gassing.
- (5) Infusion of isotonic salt solution at a time when, by hæmoglobin determinations, the blood is shown to be concentrating, and a repetition of this process at well-timed intervals, increases the chance of recovery.

It would appear therefore that "bleeding" increases the chance of survival in animals if practised before there is any conspicuous evidence that the circulation is embarrassed.

III. REVIEW OF CLINICAL EVIDENCE.

(1) *Dr. Irvine's Article in B.M.J., 1916, i, 162.*

This deals with the observations of Macaulay and others in mines in South Africa, the irritant gas being "nitrous fumes." They found out that the acute stage comes on in about six hours or somewhat later. The typical cases were cyanosed. They adopted venesection and bled 12 to 20 ozs. with considerable benefit as soon as the acute stage developed. They also adopted infusion with saline and administered oxygen intermittently. They point out that at the P.M.s of fatal cases the R. heart and the thoracic and abdominal veins were engorged with thick and sometimes "tarry" blood.

(2) *Report of Capt. A. S. Hebblethwaite, R.A.M.C. (T.F.).**

Hebblethwaite adopted venesection as routine practice in a certain class of gassed cases, viz., those of the cyanosed type, with much distress but a "good" pulse. He does not consider that bleeding "grey" cases is of advantage, because "the heart is not engorged and there is no great resistance through the lungs." On theoretical grounds he believes that:—

- (a) The resistance to be overcome by the heart is lowered in proportion to the amount of blood withdrawn.
- (b) As a result of bleeding there will be an abstraction of fluid from extra-vascular territory involving diminution of the œdema fluid in the lungs.

In practice, he found that the effects of bleeding were:—

- (a) Great relief of the cyanosis.
- (b) Relief of the pulmonary congestion, enabling the patients to breathe more easily.
- (c) Relief of the acute headache which supervenes after 24 hours.
- (d) Promotion of sleep.

Hebblethwaite thinks it is of importance to bleed "early." At the C.C.S. at which he was working the cases arrived, in one instance 14 to 18 hours, in another 18 to 36 hours, after exposure, and were markedly œdematous at the time the venesection was done. In these cases the irritant gas was probably a mixture of chlorine with a not high proportion of phosgene. In 42 cases, serious in type, venesection

* See also B.M.J., July 22, 1916, p. 107.

was performed. Of these, 12 died and 30 survived. As regards 25 of these who were followed up, 21 were in about three months marked up for full duty. In another set of 10 cases, cyanosed and all equally distressed, five were bled and did well without any further treatment; of the remainder, two died within 12 hours, three become livid and more distressed and were then bled, but required cardiac stimulants after bleeding. Hebblethwaite says that all cases bled early did well, those bled late required cardiac stimulants.

3. *Other Clinical Evidence.*

It deserves to be recorded that at the time of the first gas attacks there was no adequate means available of giving oxygen. It was the knowledge of Irvine's report that lead Lt.-Col. Douglas to suggest to Hebblethwaite that he might try venesection on his series of bad cases.

Medical authorities of the B.E.F.* hold that cases of deep cyanosis with a full pulse and signs of venous engorgement may be greatly benefited by a venesection up to 20 ozs., and that relief may be afforded at a critical period when the right side of the heart is beginning to give way under the strain; but its practice is contra-indicated in those cases which show pallor and collapse with a very rapid, thready pulse.

Herringham states his opinion that the good effects of bleeding have been verified in our own troops, and that all cases, except those which are "ashy" and those which are quite mild, should be bled to 15 ozs. at the F.A. But he expresses himself as certain that the administration of oxygen is the one great essential.

The most recent information shows that while some M.O.s are of opinion that venesection is of distinct value as a precautionary measure, and should be done as soon as there is the slightest evidence that a man has been definitely gassed and before pulmonary oedema is distinctly established, the majority regard bleeding as mainly of value in relieving venous congestion and threatening dilatation of the right heart, and take as their criterion for the necessity of bleeding the degree of embarrassment of the circulation rather than the occurrence of pulmonary oedema.

Whilst venesection gives rise in cases showing venous engorgement, associated with a full pulse of not undue rapidity, to an immediate amelioration of some of the symptoms, causing improvement of the pulse, lessened dyspnoea, and in particular, reduction of the general distress (as in Hebblethwaite's cases), it is far more difficult to ascertain in man whether precautionary venesection is really of value. The difficulty is of course mainly dependent on the fact that it is not easy to secure adequate control observations in practice: the estimate of the value of the treatment therefore must be largely a matter of personal opinion.

In order to obtain a correct idea as to the value of bleeding and as to the real indications for its practice, it is essential that the precise alteration in the symptoms which appears to result from its employment should be carefully observed and noted in a series of cases. In this

* [S.S. 452.] Memorandum on Gas Poisoning in Warfare, April, 1918.

connection the possible influence of other treatment which may be practised simultaneously (*e.g.*, oxygen inhalation) must be borne in mind. Records of arterial and venous pressures, of hæmoglobin percentage or blood counts as an index of the viscosity of the blood, or, if possible, direct determinations of the viscosity, before and for a considerable time after the venesection, would no doubt be of assistance in deciding the influence of bleeding on circulatory embarrassment.

(4) *Views of the French Medical Authorities.*

French medical authorities hold a very high opinion of the value of bleeding. "*La saignée pour l'œdème est aussi indispensable que la ligature d'une artère pour l'hémorragie.*"

They point out that the longer one waits to perform venesection the more difficult it is to bleed. They note that in cases with much cyanosis sometimes no more than 50 or 60 cc. of blood will escape. On repeating the operation in one or two hours an abundant flow may be obtained. They condemn infusion in a case menaced with œdema. In cases of acute pulmonary œdema and much dyspnoea they favour bleeding two or three times in the first 24 hours and twice a day (to the extent of 150 to 200 cc.) during the three following days. They state that the relief is such that the patients implore its repetition. In cases generally, even though the first bleeding be abundant, they recommend its repetition.

(5) *Views of the German Medical Authorities.*

In the German pamphlet on the diagnosis and treatment of gas poisoning, issued early in 1918, the following statements occur.

"A copious venesection has in many cases proved of the greatest value for checking the pulmonary œdema."

"The best remedy for the concentration of the blood is venesection."

"Besides the diminution of the viscosity of the blood the œdema of the lungs is beneficially influenced and the circulation relieved."

The Germans emphasize the necessity of removing a considerable quantity of the blood (400 to 500 cc.). As it is difficult to remove any quantity at the height of the illness, "when the blood is thick and tarry," it is advisable to venesect at an earlier stage. They recommend venesection in all moderately severe and severe cases after a preliminary injection of digitalis or strophanthin. "The effect of venesection may be assisted by a subsequent intravenous infusion of physiological salt solution." They do not consider that this accentuates the pulmonary œdema, but the results are transitory.

"Venesection is likewise indicated for the purpose of combating the disturbances of the circulation. It empties the venous system and relieves the right heart and lesser circulation. If it is practised on these grounds an immediate refilling of the vascular system by the infusion of saline solution is not indicated."

The pamphlet classifies gassed cases into :—

- (a) Mild cases.
- (b) Moderately severe cases.
- (c) Severe cases.

A differentiation into these groups is generally possible, they think, after 6 to 12 hours. The essential characteristics of the different groups are not given; there is, therefore, no direct suggestion that cyanosed cases are those that should be bled. Their conviction of the importance of venesection leads them to recommend the infusion of saline into the other arm should the blood refuse to run from the arm venesected. They even go so far as to recommend bleeding from the radial artery should venesection be ineffective.

We are not acquainted with the evidence, if any, upon which the German statements are founded, but there is some reason to believe that experimental work has been done tending to support them.

IV. CONCLUSIONS.

It is perhaps a matter for regret that more evidence does not exist at present as to the condition of blood pressure, both arterial and venous, and the degree of viscosity of the blood, especially in clinical cases. We wish to suggest that any opportunity that occurs for obtaining further information on these points should be taken advantage of. In default of such knowledge there is necessarily great difficulty in interpreting the part played by venesection. In the clinical reports it is often not easy to assess the precise value of bleeding, owing to the fact that oxygen was also employed in treatment. Nevertheless, a careful consideration of the evidence, both experimental and clinical, leads us to the firm conviction that the value of bleeding is conclusively proved for certain classes of cases gassed by pulmonary irritants. At the same time we are not satisfied that it either prevents or decreases the cedema of the lungs.

The classification of gassed cases which appears to be usually adopted is into :—

- (a) Light cases.
- (b) Cyanosed cases with venous and capillary congestion.
- (c) "Grey" or collapsed cases, in which the cyanosis is modified by the circulatory collapse and the "blueness" becomes replaced by "greyiness."

The evidence in favour of the employment of venesection in the different classes of cases seems undoubtedly to point as follows.

A. As a Therapeutic Measure.

(a) *Light Cases, not cyanosed.*—Assuming that the difficulty of clearly recognising these cases is not great, though they have at times been confused with the primarily "grey" cases, the evidence indicates that there is probably no harm in bleeding such (except that a case then becomes definitely a casualty for a time). On the other hand there is apparently no advantage and it is therefore unnecessary in practice.

(b) *Cyanosed Cases.*—"Blue" or "plum-coloured." The evidence leads to the undoubted conclusion that these cases should be bled as early as possible after the cyanosis develops. We believe that the chief value of the venesection consists in relief to an embarrassed circulation associated with threatening dilatation of the right heart.

(c) "*Grey*" or *Collapsed Cases*.—We may perhaps distinguish two groups in this class. At times a condition resembling primary shock overshadows all other symptoms and a case at once enters the class of "*grey*" cases. It is even possible that the gas or its products may exert a direct toxic action upon the circulation, leading to a condition of collapse. On the other hand there are cases which become "*grey*" as the result of failing heart secondary to venous engorgement or anoxæmia. There appears to be no evidence justifying resort to bleeding in the first group (the primarily "*grey*"). We understand that in an investigation on the employment of venesection in the gas attack mentioned by Hebblethwaite, but in units other than those dealt with by him, when the bleeding was done at a much earlier hour, the figures collected showed clearly the harmfulness of venesection in leaden-coloured cases of asphyxial collapse. How far this applies to collapsed cases that have passed through the cyanosed condition seems less certain. But probably for these cases and such as are on the border-line between classes (b) and (c) the best indication for the desirability of bleeding is the *condition of the pulse*.

B. As a Prophylactic Measure.

A short time after gassing it will generally be uncertain into which of the above categories a case will fall. Where there is reason to expect that severe symptoms will develop the experimental results appear to afford some justification for precautionary venesection.

SUPPLEMENTARY.

We have taken the opportunity to investigate certain recent work which goes to support the advantage of infusion with saline, as accessory treatment in addition to "*bleeding*."

It is claimed that it makes no increase in the degree of pulmonary oedema. The aim of the American observers who have practised it in animals is to dilute the blood when it has become concentrated and its viscosity increased. They point out that this condition is not immediate but only exhibited (after phosgene) after the lapse of some hours. They, therefore, recommend that an infusion of saline be administered at a time when the blood has become concentrated after "*bleeding*." Their statistical results are not yet complete, but on the basis of the chance of survival these results indicate considerable advantage in the treatment.

We consider that treatment by venesection and subsequent infusion has reached a stage at which the evidence from animals is sufficiently strong to justify the testing of the treatment in the field under carefully organised conditions, involving investigations on the blood pressure, the viscosity of the blood, the blood-cell count, the hæmoglobin value, and the condition of the heart.

By such observations it should be possible to ascertain what degree of concentration should warrant the employment of infusion and the time relation of the infusion to that of venesection.

The experimental evidence suggests that :—

- (a) Venesection, before concentration becomes marked, tends to modify this process, and should be practised within 10 hours of exposure to the gas.
- (b) If venesection alone is insufficient to reduce the concentration, as determined by hæmoglobin estimations, infusion of isotonic saline will help. This should be introduced in amount equal to the blood withdrawn.

(Where, owing to circulatory defects, as seen in “grey” cases, venesection is contra-indicated, a cautious employment of isotonic infusion is worthy of consideration, as experiments indicate that this does not increase the pulmonary œdema.)

July, 1918.

APPENDIX I.

THE VALUE OF VENESECTION.

By J. SHAW DUNN, Captain, R.A.M.C., and G. H. HUNT,
Captain, R.A.M.C.

(From the Porton Laboratories.)

Goats, 94 in all, were gassed in the chamber either with phosgene or chloropicrin. Half of these were controls, the other half were bled from the jugular vein to the extent of 1/160 of the body weight. The doses, times of exposure, and other data are given in the tables below. The experiments form two series :—

- (a) In which the animals were taken without any selection.
- (b) Those in which a clinical examination was made before venesection to secure that the animals bled and the controls had lungs equally injured by the gas.

At stated times after the gassing the animals were killed, and the tables show a comparison between the post-mortem conditions of the lungs of the bled and unbled gassed animals.

Table Showing Results of Experiments.

No. of experiment.	No. of goats used.	Gas.	Duration of exposure in minutes.	No. of goats dying.	No. of hours after gassing that venesection was done.	No. of hours after gassing that goats were killed.	Bled goats.		Control goats.		Remarks.
							Good lungs.	Bad lungs.	Good lungs.	Bad lungs.	
F. 1. ...	8	2 c.c. chloropicrin	30	0	1-3	3½	1	3	2	2	Not selected.
F. 1 ...	4	2 c.c. "	30	0	3	6	2	0	0	2	Not selected.
F. 2 ...	7	2 cc. "	30	1	1-3	6	1	3	2	1	Not selected.
F. 2 ...	5	2 cc. "	30	0	1-3	24	0	2	0	3	Not selected.
F. 11 ...	10	5 cc. phosgene	30	2	1	48	2	3	2	3	Selected.
	34						6	11	6	11	Totals giving results of bleeding within three hours after gassing.
F. 3 ...	8	2 cc. chloropicrin	30	1	6	27	3	1	1	3	Not selected.
F. 6 ...	10	2 cc. "	30	0	6	23	0	5	2	3	Not selected.
F. 7 ...	10	2 cc. "	20	0	6	24	2	3	2	3	Selected.
F. 14 ...	10	3 cc. phosgene	20	4	6	48	3	2	3	2	Selected.
	38						8	11	8	11	Totals giving result of bleeding six hours after gassing.
F. 4 ...	4	2 cc. chloropicrin	30	0	24	48	1	1	1	1	Not selected.
F. 5 ...	7	2 cc. "	30	0	24	48	1	3	2	1	Not selected.
F. 13 ...	8	4½ cc phosgene	20	1	24	48	1	3	1	3	Selected.
F. 12 ...	5	4½ cc "	30	0	24	48	1	1	1	2	Selected.
	24						4	8	5	7	Totals giving results of bleeding twenty-four hours after gassing.
	96						18	30	19	29	Grand Totals.

CONCLUSION.

In the aggregate the lungs of animals which were bled were no better than the controls.

APPENDIX 2.

EXPERIMENTS TO DETERMINE WHETHER VENESECTION HAD ANY THERAPEUTIC VALUE IN GOATS GASSED WITH SMALL DOSES OF CHLOROPICRIN AND PHOSGENE.

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Captain, R.A.M.C.

(From the Porton Laboratories.)

Method of Experiment.

Goats were gassed in the chamber for 15—20 minutes. They were then examined, and divided into groups according as they were slightly or severely affected. Half the goats in each group were used as controls, and half were bled six hours after gassing. The animals were selected in this way as there is great variation in the degree to which different goats are affected by the same dose of gas. Bleeding was done through a cannula inserted into the jugular vein, and one ounce of blood was removed for every 10 pounds body weight.

Forty-eight hours after gassing all the goats were killed and their lungs examined; these were divided into three groups as follows:—

- (i) Very œdematous lungs (marked “Bad” in the table).
- (ii) Moderately œdematous lungs (marked “Moderate” in the table).
- (iii) Slightly œdematous lungs (marked “Good” in the table).

The heart and lungs were weighed in every case, and the average “heart-lung ratio” of the bled and control goats in each experiment estimated.

The results are given in the table at the end. In the first experiment there was a decided balance in favour of venesection, but this was not the case in the last two experiments, where there was nothing to choose between the lungs of the bled and control goats. On the whole, the evidence was very slightly in favour of venesection, but it was not sufficiently strong to be of any significance.

TABLE.

Expt.	No. of goats.	Dose.	*Condition of lungs in bled goats.			Condition of lungs in control goats.			Average heart-lung ratio.	
			Bad.	Mod.	Good.	Bad.	Mod.	Good.	Bled goats.	Controls
F.34 ...	10	3 cc. phosgene for 15 m.	0	3	2	2	3	0	2.70	4.60
F.35 ...	10	1 c.c. chloropicrin for 20 m.	0	2	3	0	2	3	2.58	2.34
F.36 ...	10	1 cc. chloropicrin for 20 m.	0	3	2	0	3	2	2.64	2.34
Total	30		0	8	7	2	8	5	2.64	3.09

* In the experimental chamber 3 cc. phosgene = 1/10500.
1 cc. chloropicrin = 1/43500.

November 29th, 1917.

APPENDIX 3.

THE EFFECTS OF VENESECTION AND INFUSION OF SALINE AFTER IRRITANT GAS POISONING.

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I. CHLORINE.

The value of venesection as a general treatment of men gassed with lung irritants has been the subject of considerable discussion. The clinical data are very fragmentary. Combined with this, the absence of experimental evidence showing that bleeding is a valuable therapeutic procedure for gassed animals has permitted legitimate doubts to be entertained concerning the efficacy of this method of treatment.

So far as the knowledge of the authors is concerned, the first positive experimental results were obtained by the Division of Intermediary Metabolism of the United States Gas Investigations, in dogs gassed with lethal concentrations of chlorine. This investigation was

conducted under the leadership of Professor F. P. Underhill, and the authors took an active part throughout. Dogs were severely gassed with carefully controlled concentrations of chlorine and treated within 1 to 2 hours after the exposure to the gas. Bleeding was performed to the extent of 1 per cent. of the body weight of the animal. The following table gives the results of these experiments.

TABLE I.—*Effect of Bleeding in Dogs Gassed with Chlorine.*

(800–900 parts per million—1 : 1250 to 1 : 1100 for 30 mins.)

			Acute deaths.	Delayed deaths.	Survivals.	Animals used.
			Per cent.	Per cent.	Per cent.	
Untreated	...	...	87	4	9	23
Bled	...	...	65	5	30	20

In these experiments, as well as those in Table II, three days were taken as the limit of the time in which death occurred from the acute effects of the gassing. This seemed justifiable, since most of the deaths occurred during the first 48 hours. Thereafter the deaths were few and usually due to secondary causes, most often, pneumonia of a purulent type. It will be seen from the above table that bleeding alone reduced the acute deaths in dogs gassed with lethal concentrations of chlorine from 87 per cent. to 65 per cent., and increased the survivals from 9 per cent. to 30 per cent. Under the extremely well controlled conditions of the investigation we believe that these figures are significant and indicate the value of bleeding in animals gassed with chlorine.

Infusion of isotonic salt solution and the administration of sodium bicarbonate after bleeding was found to yield still better results, as shown in the following table.

TABLE II.—*Effect of Bleeding, Infusion of Isotonic Salt Solution and Administration of Alkali in Dogs Gassed with Chlorine.*

(800–900 parts per million—1 : 1250 to 1 : 1100 for 30 mins.)

			Acute deaths.	Delayed deaths.	Survivals.	Animals used.
			Per cent.	Per cent.	Per cent.	
Untreated	...	...	87	4	9	23
Treated	...	...	53	23	24	62

Discussion of Table II.

Bleeding to the extent of 1 per cent. of the body weight of the animal, followed by intravenous infusion of warm sterile .95 per cent. sodium chloride solution, and the administration of sodium bicarbonate by mouth decreased the acute deaths from 87 per cent. to 53 per cent., and increased the complete survivals from 9 to 24 per cent. We believe that the decrease in the percentage of acute deaths from 87 per cent. to 53 per cent. is significant, even though a considerable group of animals died after the 3-day period. These delayed deaths are due to secondary causes and not to the *direct* effect of the gas, and must for this reason be considered outside the scope of the present work. This treatment is therefore more beneficial than bleeding alone when applied to dogs severely gassed with chlorine.

On the basis of these experimental data which are briefly presented above, it seemed most advisable to pursue the investigations further upon other gases of the class of lung irritants now in use in warfare.

Through the kindness of General H. F. Thuillier we (S.G. and D.W.W.) were given the use of the facilities of the Physiological Laboratories at the R.E. Experimental Station, Porton, England. We take this occasion to express our sincere gratitude to Mr. Barcroft and his associates at Porton for this privilege and for their many kindnesses extended to us throughout the investigation, which we, in part, report herewith.

II. CHLORPICRIN.

Method of Gassing and Technique of Experimental Methods.

The method of gassing may be outlined briefly. Ten or twelve animals were placed in the gassing chamber and left for a period of 25 minutes in an atmosphere of chlorpicrin, made by spraying in the liquid in quantities sufficient to develop a theoretical concentration of from one part of chlorpicrin in 8500 to 9000 parts of air. The air in the chamber was kept continually in motion during the period of the gassing by means of an electric fan.

Goats were used exclusively in these experiments.

The animals were arbitrarily divided into two equal groups; one group was treated, while the other served as a control. An effort was made to have, so far as possible, an equal division of animals as regards weight and sex, in the two groups. This division was made without any reference to the animal, before the gassing was completed, and adhered to regardless of the condition of the respective animals after the gassing.

Bleeding was performed by aspiration through a needle inserted through the skin into the right or left jugular vein. This procedure was performed so far as practicable under aseptic precautions.

One bleeding only was made one hour after the animals were removed from the chamber.

All of the animals which survived were kept under careful observation for a period of 5 to 7 days, and then sacrificed for post-mortem

examination. As nearly 90 per cent. of the mortalities occurred within the first 24 hours, and most of the surviving animals improved rapidly thereafter, the length of the period of observation is considered ample. Hence we may safely state that life or death has been our criterion of the beneficial effect of the treatment employed.

A large number of experiments were performed, but for the purpose of this report only those groups in which from 60 to 100 per cent. of the goats in the control group died are chosen. The treatment of animals gassed at lower concentrations will be the subject of a later communication.

The following tables give the results of these experiments.

TABLE III.—*Effect of Bleeding in Goats Gassed with Chlorpicrin.*

(1 : 8500 to 1 : 9000 for 25 mins.)

	Animals used.	Deaths.	Percentage Deaths.
			Per cent.
Untreated	48	43	90
Treated	47	27	57

TABLE IV.—*Effect of Bleeding in Goats Gassed with Chlorpicrin.*

(1 : 8500 to 1 : 9000 for 25 mins.)

Animals grouped according to time of death.

	3-8 hours.	8-24 hours.	24-48 hours.	2-7 days.	Total deaths.	Survivals.
Untreated	19	18	2	4	43	5
Treated	8	16	1	2	27	20

Animals surviving at beginning of period :—

Untreated	48	29	11	9
Treated	47	39	23	22

Percentage deaths among animals surviving at beginning of period :—

	Per cent.	Per cent.	Per cent.	Per cent.
Untreated	40	62	18	44
Treated	17	41	4	9

Discussion of Results.

As may be seen in Table III above, the mortality of the treated animals is decreased from 90 to 57 per cent. by a single bleeding in a severely gassed goat. This large reduction in mortality in the 95 animals used in these experiments demonstrates conclusively that

bleeding is an efficacious therapeutic procedure when applied early to goats gassed with high concentrations of chlorpicrin.*

Table IV shows the percentage of deaths (expressed as per cent. of animals surviving at the beginning of each period) of experimental and control animals at four periods after gassing. The first critical period occurs within eight hours after gassing. An inspection of Table IV shows that whereas 40 per cent. of the control animals had died at this time but 17 per cent. of the treated animals succumb at this period.

The next and more critical period lies between 8 and 24 hours. Here also a greater percentage of the untreated animals die. Hence a single treatment has furnished protection for the treated animals through the severest of the acute stage of the gassing. After 24 hours the number of treated animals which die is very small; on the other hand the untreated continue to give an appreciable percentage of deaths. We may therefore conclude that the treatment has given a permanent advantage, and has not merely delayed the death of the animal.

III. PHOSGENE.

As in the chlorine experiments given above, dogs were gassed in an atmosphere of phosgene for 30 minutes. The concentration was kept at a constant level throughout the gassing by passing the gas mixed with air at a fixed rate through the chamber. Chemical analyses served as a further check upon the concentration during the period of gassing. By this method is obtained a standard gassed animal, and it has been found that the toxicity percentages are certainly accurate within 10 per cent., which covers merely the individual variation in the animals. The following table gives the results of bleeding alone.

TABLE V.—*Effect of Bleeding in Dogs Gassed with Phosgene.*
(71–80 parts per million—1 : 14,200 to 1 : 12,500 for 30 mins.)

	Deaths.			Total Acute Deaths.	Delayed Deaths.	Sur- vivals.	Animals used.
	24 hours.	2nd day.	3rd day.				
	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	
Untreated ...	38	21	10	69	10	21	29
Bled 1 hour after gassing	27	13	—	40	10	50	30
Bled 5 hours after gassing	33	10	—	43	10	47	30

Discussion of Table V.

The above figures show that one bleeding to the extent of 1 per cent. of the body weight either one hour or five hours after gassing produces equally good results with concentrations producing 78 per

* These data have been subjected to statistical analysis and found to be conclusive.

cent. mortality in untreated animals. The acute deaths are reduced from 67 per cent. in untreated animals to 40 per cent. in treated. The recoveries increased from 22 per cent. in untreated to 50 per cent. in the treated. These figures are sufficiently significant to show that in dogs gassed with phosgene bleeding has an undoubted beneficial effect.

Effect of Multiple Small Bleedings.

It is of extreme importance to know whether multiple small bleedings would prove as beneficial as a single large bleeding. The following table gives the results of this method of treatment at three different concentrations.

TABLE VI.—*Effect of Multiple Small Bleedings in Dogs Gassed with Phosgene at various concentrations.*

	Deaths.			Total Acute Deaths.	Delayed Deaths.	Sur- vivals.	Animals used.
	24 hours.	2nd day.	3rd day.				
Gassed with phosgene 61-70 parts per million (1 : 16,400 to 1 : 14,300) for 30 mins. :—							
	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	
Untreated ...	20	25	—	45	10	45	20
Bled... ..	9	—	9	18	9	63	11
Gassed with phosgene 71-80 parts per million (1 : 14,200 to 1 : 12,500) for 30 mins. :—							
Untreated ...	37	22	7	67	11	22	27
Bled ...	23	15	23	62	7	31	13
Gassed with phosgene 81-90 parts per million (1 : 12,400 to 1 : 11,000) for 30 mins. :—							
Untreated ...	50	12	—	61	15	23	26
Bled... ..	45	27	9	82	—	18	11

Discussion of Table VI.

In concentrations producing a mortality of about 50 per cent. in the untreated animals (61–70 parts of phosgene per million parts of air for 30 minutes) bleeding in small amounts at intervals shows a very decided beneficial effect. As the concentration is increased it will be seen that the beneficial effect of this form of treatment becomes progressively less. The apparent harmful effect at 81–90 calls for a word of explanation. In a severely gassed animal under experimental conditions, the annoyance and excitement caused by the act of subjecting it to treatment is considerable, and therefore unless the beneficial effects far overshadow this undoubted harmful effect of excitement, results such as are obtained in series three above will be

obtained. From the combined results in Tables V and VI above, and also as indicated by some preliminary results which were started independently by us here, it seems justifiable to make the preliminary statement that heavily gassed animals require early and heavy treatment preferably, while comparatively lightly gassed animals may be treated by bleeding at intervals in small amounts.

That this should logically be the case is borne out by the following facts. In an animal severely gassed the development of the fatal symptoms would occur very early, therefore treatment is indicated early. As the gassing becomes less severe, as is shown by pathological investigations, with all three lung irritants, chlorine, chlorpicrin and phosgene, the development of fatal symptoms becomes less rapid.

Effect of Bleeding and Infusion.

Inasmuch as a combination of bleeding followed by infusion of isotonic sodium chloride solution gave better results in the treatment of animals gassed with chlorine, the same procedure was applied to dogs gassed with phosgene. The following table gives the results of this method of treatment. Both the bleeding and the infusion were performed one hour after gassing.

TABLE VII.—*Effect of Bleeding and Early Infusion in Dogs Gassed with Phosgene.*

(71–80 parts per million—1 : 14,200 to 1 : 12,500 for 30 mins.)

	Deaths.			Total Acute Deaths.	Delayed Deaths.	Sur- vivals.	Animals used.
	24 hours.	2nd day.	3rd day.				
Untreated ...	Per cent. 38	Per cent. 21	Per cent. 10	Per cent. 69	Per cent. 10	Per cent. 21	29
Treated ...	40	3	3	50	3	47	30

Discussion of Table VII.

Bleeding one hour after gassing to the extent of 1 per cent. of the body weight followed immediately by an infusion of an equal quantity of isotonic sodium chloride solution yielded results in the first 24 hours less satisfactory than bleeding alone. This led to the experimentation described below which has yielded a course of treatment more successful than any hitherto obtained. It is of interest to note that of the 50 per cent. of the animals surviving the acute period but 3 per cent. die subsequently, against 10 per cent. of the untreated animals.

Bleeding and Delayed Infusion.

It is well known that immediately after gassing with chlorine there is a concentration of the blood. Upon investigation of dogs gassed with phosgene it was found that in the first four hours after gassing

the blood has a distinct tendency to be more dilute than normal, but later, depending upon the severity of the gassing, the blood becomes concentrated. At concentrations of 70-80 parts per million this concentration occurs at about the eighteenth hour after gassing; above 80 parts per million the blood becomes thick sooner, about 15 hours after gassing. On the basis of this result it was decided to test the value of bleeding 1 per cent. of the body weight one hour after gassing and delay infusion until 15-20 hours after gassing. The results are tabulated below in two ways. First, the total number of animals treated by bleeding and infusion including those animals which die before the infusion, are compared with animals not treated and with another group treated by bleeding only. Second, in each group a percentage of animals equivalent to the animals which die before infusion is eliminated. This is done to determine whether infusing increases the expectation of life.

TABLE VIII.—*Effect of Bleeding and Delayed Infusion in Dogs Gassed with Phosgene.*

(71-80 parts per million—1 : 14,200 to 1 : 12,500 for 30 mins.)

	Deaths.			Total Acute Deaths.	Delayed Deaths.	Sur- vivals.	Animals used.
	24 hours.	2nd day.	3rd day.				
	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	
Untreated ...	38	21	10	69	10	21	29
Bleeding only	27	13	—	40	10	50	30
Bleeding and Delayed Infusion ...	—*						
	14†	14	3	31	17	52	35
14 per cent. early deaths eliminated from each group.							
Untreated ...	28	24	12	64	12	24	25
Bleeding only	15	15	—	31	11	58	26
Bleeding and Delayed Infusion ...	—	17	3	20	20	60	30

* Before Infusion.

† After Infusion.

Discussion of Table VIII.

The method of treatment adopted herewith, bleeding in one hour to the extent of 1 per cent. of the body weight followed by infusion of isotonic sodium chloride solution 15-20 hours after gassing yielded the following results. Considering the first grouping: during the most critical period, namely the first 24 hours, the deaths are decreased from 38 per cent. in the untreated animals to 14 per cent. in the treated animals. It is also evident that infusion has added to the value of bleeding since in this same period the deaths with bleeding alone amount to 27 per cent. against 14 per cent. when the animals are also infused. From this it is clearly indicated that infusion has had a

beneficial effect during the very acute period. Now passing to our second classification where a number of animals equivalent to those which die before infusion are eliminated from the three groups. Further evidence of the immediate value of infusion is indicated by the fact that whereas 15 per cent. of the animals die in the first 24 hours when bled only, none of the animals which are infused die in this period. By this method of grouping also, a preliminary idea of the post acute value of infusion may be obtained. Here it is evident that the total number of acute deaths has been reduced from 64 per cent. in the untreated to 31 per cent., when bled only; to 20 per cent. when bled *and infused* with isotonic salt solution after 15–20 hours; further evidence that infusion is of value during the whole acute stage. The total recoveries are of the same order in bleeding alone and bleeding and infusion in these experiments, but we shall show in subsequent tables how this lead is developed and the evidence strengthened to prove the value of infusion. There can be no doubt that so far the length of life of the animals which die is considerably lengthened.

Bleeding and Delayed Infusion in Animals Gassed at a higher concentration of Phosgene.

One thing stands out in phosgene poisoning, namely, that in general the higher the concentration of gas to which an animal is subjected the sooner do the toxic symptoms appear. That is, the more rapid is the onset of acute death. It is also found that the concentration of the blood appears earlier at these higher concentrations. Therefore, theoretically, infusion for the purpose of diluting the blood should be performed earlier. The following data give the results of bleeding one hour after gassing at concentrations of 80–90 parts of phosgene per million parts of air followed by infusion 10 hours after the gassing. Here also the data is grouped in two ways as above.

TABLE IX.—*Effect of Bleeding and Delayed Infusion (10 hours) in Dogs Gassed with Phosgene at higher concentration.*

(80–90 parts per million—1 : 12,500 to 1 : 11,100 for 30 mins.)

	Deaths.			Total Acute Deaths.	Delayed Deaths.	Sur- vivals.	Animals used.
	24 hours.	2nd day.	3rd day.				
Untreated ...	Per cent. 54	Per cent. 10	Per cent. 3	Per cent. 67	Per cent. 13	Per cent. 20	30
Bleeding and Delayed Infusion ...	23* 14†	14	3	54	6	40	35
23 per cent. early deaths eliminated from each group.							
Untreated ...	39	13	4	57	17	26	23
Bleeding and Delayed Infusion ...	19	19	3	41	7	52	27
Before Infusion.				† After Infusion.			

Discussion of Table IX.

Here also the general features of Table VIII are repeated. There is an undoubted reduction of the acute deaths especially in the very early period.

Bleeding and Infusion at the Proper Time as Indicated by Hæmoglobin Determinations.

The general thesis that infusion should be resorted to when the blood shows a tendency to become thickened has now been followed to a logical conclusion. It is found that simple hæmoglobin determinations (the Tallquist hæmoglobinometer is sufficiently accurate) can be used as an index of this concentration. A group of animals have therefore been gassed at a concentration of 80-90 parts of phosgene per million parts of air, bled one hour after gassing and as the blood showed concentration infusion was resorted to and repeated as required. The initial infusion should not be delayed in any case beyond the time when the blood has reached a concentration more than 25 per cent. above normal. A second infusion is indicated when the hæmoglobin shows a concentration of 40 per cent. above normal. The treatment should not be carried out too frequently. At this stage as long as the concentration of the blood does not increase, further infusion is unnecessary. The following table gives the preliminary results of this method of treatment, compared with the simple mass treatment at the same concentration.

TABLE X.—*Effect of Bleeding and Infusion at the Proper Time as Indicated by Hæmoglobin Determinations in Dogs Gassed with Phosgene.*

(80-90 parts per million—1 : 12,500 to 1 : 11,100 for 30 mins.)

23 per cent. early deaths eliminated from first two groups.*

	Deaths.			Total Acute Deaths.	Delayed Deaths.	Sur- vivals.	Animals used.
	24 hours.	2nd day.	3rd day				
Untreated ...	39	13	4	57	17	26	23
Bleeding and Delayed Infusion ...	19	19	3	41	7	52	27
Bleeding and Infusion at Proper Time ...	—	—	—	22	5	73	22

* At this writing we are uncertain whether in this compilation early deaths were eliminated, hence we present the data as if this were the case, putting them therefore in the worst possible light.

Discussion of Table X.

This table shows conclusively that when the concentration of the blood is followed by the hæmoglobin content and the time of infusion is properly ascertained, in addition to the great reduction of acute deaths heretofore demonstrated, the percentage of total recoveries is markedly increased—from 26 per cent. in the untreated group to 52 per cent. in the group where the time of infusion was not accurately correlated with blood concentration (infusion usually being about 10 hours after gassing) to 73 per cent. when the time of infusion was properly ascertained. In the communication from which these data are taken, it is pointed out that but one delayed death occurred which may mean that the treatment has a tendency to prevent secondary infection, a significant point when dogs are the experimental animals. The theoretical considerations and the experimental data on which this method of treatment is founded will not be taken up here but will constitute the subject of a later communication.

IV. DISCUSSION OF BLEEDING AS A METHOD OF TREATMENT FOR POISONING WITH CHLORINE, CHLORPICRIN AND PHOSGENE.

It has been conclusively demonstrated in three typical examples of the class of lung irritants that bleeding has a beneficial effect. It seems permissible therefore to assume that this method of treatment might allow of general application in counteracting the effects of gases which produce as their chief symptoms cedema and congestion of the lungs. As a preliminary recommendation for man, we should suggest that early bleeding be performed when possible, especially in severely gassed cases.

V. DISCUSSION OF INTRAVENOUS INFUSION OF ISOTONIC SALT SOLUTION AS AN ACCESSORY TREATMENT TO BLEEDING.

On the basis of results obtained in both chlorine and phosgene poisoning, infusion of isotonic salt solution, at the period when the blood concentrates, gives better results than simple bleeding. The value of the accessory infusion of isotonic salt solution is proved beyond doubt in dogs gassed with lethal concentrations of phosgene, bled one hour after the gassing, and infused as hæmoglobin determinations on the individual animal indicated concentration of the blood.

In addition to the experiments given above, we wish to present here, very briefly, the results of an investigation which bears directly upon the question of infusion. A series of dogs were exposed to graded concentrations ranging from 41 to 50; 51 to 60; 61 to 70; and 71 to 80 parts of phosgene per million of air. The length of exposure was 30 minutes. Twenty dogs were gassed at each of these concentrations of phosgene. As indicated by hæmoglobin and total solid determinations (these give parallel curves), it was found that the concentration of the blood is an index of the severity of the gassing. Furthermore, the animals that died acutely have, invariably, a blood concentration curve which tends to assume a vertical course.

Hence we must conclude that a concentration of the blood is contributory to a fatal outcome. Treatment of this condition is most certainly indicated. Intravenous infusion of isotonic salt solution into experimental animals at this stage has been definitely shown to increase the chances of recovery.

CONCLUSIONS.

1. Bleeding is beneficial for animals gassed with any of the three typical examples of the class of lung irritants, chlorine, chlorpicrin or phosgene.

2. Bleeding followed by accessory infusion of isotonic salt solution at a time when, by hæmoglobin determinations, the blood is shown to be concentrating, and a repetition of this process at well-timed intervals, increases the chances of recovery.

3. In so far as animal experiments may indicate, general application of these procedures to gassed men seems justifiable.



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